

AMENDMENTS TO THE SPECIFICATION

In the application:

Please add to the application the Sequence Listing containing 58 pages submitted under 37 C.F.R. §§1.821-1.825.

In the specification:

Please replace paragraph [0051], beginning on page 13 with the following paragraph:

--For example, a native synthesized BoNT/A can comprise: MPFVNKQFNYKD, (SEQ ID NO:123) whereas a native processed BoNT/A can comprise PFVNNQFNYKD (SEQ ID NO:124). Thus a proposed 8 amino acid deletion would retain the YKD amino acid residues, while a recombinantly produced deletion would retain the MYKD (SEQ ID NO:125) amino acid residues.--

Please replace paragraph [00113], beginning on page 26 with the following paragraph:

--In one embodiment, the leucine-based motif is xDxxxLL, (SEQ ID NO:126) wherein x can be any amino acids. In some embodiments, the leucine-based motif is xExxxLL, (SEQ ID NO:127) wherein E is glutamic acid. In some embodiments, the duplet of amino acids can include an isoleucine or a methionine, forming xDxxxLI (SEQ ID NO:128) or xDxxxLM, (SEQ ID NO:129) respectively. Additionally, the aspartic acid, D, can be replaced by a glutamic acid, E, to form xExxxLI, (SEQ ID NO:130) xExxxIL (SEQ ID NO:131) and xExxxLM (SEQ ID NO:132). In a suitable embodiment, the leucine-based motif is phenylalanine-glutamate-phenylalanine-tyrosine-lysine-leucine-leucine, SEQ ID NO:1.--

Please replace paragraph [00140], beginning on page 34 with the following paragraph:

--Tyrosine-based motifs are within the scope of the present invention as biological persistence and/or a biological activity altering components. Tyrosine-based motifs comprise the sequence Y-X-X-Hy (SEQ ID NO:133) where Y is tyrosine, X is any amino acid and Hy is a

hydrophobic amino acid. Tyrosine-based motifs can act in a manner that is similar to that of leucine-based motifs. In Fig. 3 some of tyrosine motifs found in the type A toxin light chain are bracketed. In addition, a tyrosine-based motif is found within the leucine-based motif which is indicated by an asterisked bracket in Fig. 3.--

Please replace paragraph [00143], beginning on page 34 with the following paragraph:

--Fig. 8 shows a sequence alignment between type A and type B light chains isolated from strains type A HallA (SEQ ID NO:24 and SEQ ID NO:25) and type B Danish I (SEQ ID NO:26 and SEQ ID NO:27) respectively. Light chains or heavy chains isolated from other strains of botulinum toxin types A and B can also be used for sequence comparison. The shaded amino acids represent amino acid identities, or matches, between the chains. Each of the shaded amino acids between amino acid position 10 and amino acid position 425 of the Fig. 8 consensus sequence, alone or in combination with any other shaded amino acid or amino acids, represents a biological persistence altering component that is within the scope of the present invention. For example, amino acids KAFK at positions 19 to 22, LNK at positions 304 to 306, L at position 228 in combination with KL at positions 95 and 96, FDKLYK at positions 346 to 351, YL-T at positions 78 to 81, YYD at positions 73 to 75 in combination with YL at positions 78 and 79 in combination with T at position 81, F at position 297 in combination with I at position 300 in combination with KL at positions 95 and 96 can be biological persistence altering components for use within the scope of this invention. In addition, conserved regions of charge, hydrophobicity, hydro-philicity and/or conserved secondary, tertiary, or quaternary structures that may be independent of conserved sequence are within the scope of the present invention.--

Please replace paragraph [00275], beginning on page 64 with the following paragraph:

--Additional studies showed that a GFP-LCA construct with eight amino acid residues (PFV NKQFN) (SEQ ID NO:135) deleted from the N-terminus (no C-terminus deletion) localized in PC12 cells a very similar pattern to the localization in PC12 cells of a truncated GFP-LCA construct with both the C and N terminus deletions.--

Please replace paragraph [00276], beginning on page 64 with the following paragraph:

--Further studies showed that a GFP-LCA construct with twenty two amino acid residues (KNFTG LFEFYKLLCV RGIITSK) (SEQ ID NO:136) deleted from the C-terminus (no N-terminus deletion) localized in PC12 cells in a very similar manner to that of the GFP-LCA(LL-->AA) mutant.--

Please replace paragraph [00277], beginning on page 64 with the following paragraph:

--A GFP-LCA construct with both eight amino acid residues (PFVНКQFN) (SEQ ID NO:135) deleted from the N-terminus and twenty two amino acid residues (KNFTG LFEFYKLLCV RGIITSK) (SEQ ID NO:136) deleted from the C-terminus accumulated intracellularly.--

Please replace paragraph [00278], beginning on page 65 with the following paragraph:

--The first 30 residues of the amino-terminus (N-term) and the last 50 residues of the carboxyl-terminal (C-term) of the amino acid sequences of botulinum toxin serotypes A through G light chains (LC) are shown in Table 2.

Table 2

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	MPFVNKQFNYPKDPVN GVDIAYIKIPNAGQM	GFNLRTNLAANFNGQNTNINMNF TKLKNFTGLFEFYKLLCVRGIITSK	<u>14/15</u>
BoNT/B	MPVTINNFNYNDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKAI NKQAYEEISKEHLAVYKIQMCKSVK	<u>16/17</u>
BoNT/C1	MPITINNFNYSDPVDN KNILYLDTHLNTLA	NIPKSNLNVLFMGQNLNRPALRKV NPENMLYLFTKFCHKAIDGRSLYNK	<u>18/19</u>
BoNT/D	MTWPVKDFNYSDPVN DNDILYLRIQNKLI	YTIRDGFNLTKGFNIENSGQNIERN PALQKLSSSVVDLFTKVCLRLTK	<u>20/21</u>
BoNT/E	MPKINSFNYNDPVNDR TILYIKPGGCQEFY	GYNINNLKVNFRGQANLNPRIITPIT GRGLVKKIIRFCKNIVSVKGIRK	<u>22/23</u>
BoNT/F	MPVAINSFNYNDPVN DDTILYMQIPYEEKS	TVSEGFNIGNLAVNNRGQSIKLNPKII DSIPDKGLVEKIVKFKSVIPRK	<u>24/25</u>
BoNT/G	MPVNIKXFNYNDPINN DDIIMMEPFNDPGP	QNEGFNIASKNLKTEFNGQNKAVNK EAYEEISLEHLVIYRIAMCKPVMYK	<u>26/27--</u>

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Please replace paragraph [00280], beginning on page 65 with the following paragraph:

--Examples of amino acid sequence substitutions include the replacement of one or more contiguous or non-contiguous amino acids in the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain with an equal number and placement of amino acids that differ from the wild-type sequence. Substitutions can be conservative or non-conservative of the character of the amino acid. For example, the amino acid valine at a specific position in the wild-type sequence can be replaced with an alanine in the same position in the substituted sequence. Furthermore, basic residues such as arginine or lysine can be substituted for highly hydrophobic residues such as tryptophan. A proline or histidine residue may be substituted in order to form or disrupt a potentially important structural or catalytic element of the protein. Some examples of amino acid substitutions are indicated by bold underlined text in the sequences described in Table 3.

Table 3

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	MPF <u>A</u> NKQFNYKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNT <u>E</u> INNM N <u>R</u> TKLKNFTGLFEFYKLLCVRGIIT SK	<u>28/29</u>
BoNT/A	MPFVNKQF <u>N</u> KKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNT <u>E</u> INNM NFTKLK <u>N</u> A <u>A</u> GLFEFYKLLCVRGIIT SK	<u>30/31</u>
BoNT/A	MPFVNKQFNYKDPVN GVDI <u>A</u> R <u>I</u> KIPNAGQM	GFNLRNTNLAAN <u>H</u> NGQNT <u>E</u> INNM NFTKLKNFTGLFEFYKLLCVRGIIT SK	<u>32/33</u>
BoNT/A	MPFVN <u>K</u> <u>H</u> FNYKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNT <u>E</u> INNM NFTKLKNFTGLFEFYKLL <u>C</u> ARGIIT SK	<u>34/35</u>
BoNT/B	MP <u>A</u> TINNFNYNDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAYEEISKEHLAVYK <u>I</u> RMCKS VK	<u>36/37</u>
BoNT/B	MPVTINNFNYNDPIDN DNI <u>A</u> <u>A</u> EPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAYEEISKEHLAV <u>R</u> KIQMCKS VK	<u>38/39</u>
BoNT/B	MPVTINNF <u>N</u> <u>R</u> NDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQ <u>A</u> <u>K</u> EEISKEHLAVYKIQMCKS VK	<u>40/41</u>
BoNT/C1	MPITIN <u>N</u> <u>K</u> NYSDPVDN KNILYLDTHLNTLA	NIPKSNLNVLFMGQNLSRNPALRK VNPENMLYLFTKFCHKAIDGR <u>S</u> <u>L</u> <u>R</u>	<u>42/43</u>

		NK	
BoNT/D	MTWP <u>A</u> KDFNYSDP <u>A</u> N DNDILYLRI PQNKLI	YTIRDGFNLTNKGFNIE NSGQNIER NPALQKLSSSVVDLFTK <u>A</u> CLRLT K	<u>44/45</u>
BoNT/E	MPKINSFNYNDP <u>A</u> NDR TILYIKPGGCQEFY	GYNINNLKVNFRGQANLNPRIITP ITGRG <u>H</u> VKKIIRFCKNIVSVKGIRK	<u>46/47</u>
BoNT/E	MPKINSRNYNDPVND RTILYIKPGGCQEFY	GYNINNLKVNFRGQANLNPRIITP ITGRGLVKKIIRFCKN <u>A</u> ASVKGIRK	<u>48/49</u>
BoNT/E	MPKINSFNYNDPVNDR TILYIKPGGCQEF <u>R</u>	GYNINNLKVNFRGQANLNPRIITP ITGRGLVKKIIRFCKNIVS <u>A</u> KGIRK	<u>50/51</u>
BoNT/F	MP <u>A</u> AINSFNYNDPVN DDTILYMQIPYEEKS	TVSEGFNIGNLAVNNRGQSIKLN KIIDSIPDKGLVEKIVKFKS <u>A</u> IPRK	<u>52/53</u>
BoNT/G	MPVNIKX <u>H</u> NYNDPIN NDDIIMMEPFNDPGP	QNEGFNIASKNLKTEFNGQNKAVN KEAYEEISLEHLVIYRIAMCKP <u>A</u> M YK	<u>54/55</u> --

Please replace paragraph [00281], beginning on page 67 with the following paragraph:

--Examples of amino acid sequence mutations include changes in the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain sequence such that one or several amino acids are added, substituted and/or deleted such that the identity, number and position of amino acids in the wild-type light chain sequence is not necessarily conserved in the mutated light chain sequence. Some examples of amino acid sequence mutations are described in Table 4, in which additions of amino acids are shown in bold underlined text, and deletions are indicated by dashes in the sequences shown.

Table 4

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	MPFVNKQFNYKDPVN GVDIAYIKIP <u>H</u> ----	GFNLRNTNLAANFNGQNT EINN M <u>NAAAAAAAAA</u> -----CVRGIITSK	<u>56/57</u>
BoNT/A	<u>MAAA</u> ---- NYKDPVNGVDIAYIKI PNAGQM	<u>G</u> KNLRNTNLAANFNGQNT EINN M NFTKLKNFTGLFEFYK— CVRGIITSK	<u>58/59</u>
BoNT/A	MPFVNKQFNYKDPVN GVDIAR <u>R</u> ----NAGQM	GFNLRNTNLAA---- <u>H</u> NTEINN MNFTKLKNFTGLFEFYK LLCVRGIITSK	<u>60/61</u>

BoNT/A	MPKVNKQFN--- VNGVDIAYIKIPNAGQ M	GFNLRNTNLAANFNGQNTTEINNM NFTKLKNFTGLFEFRR-----TSK	<u>62/63</u>
BoNT/B	MPVTINNFNYNDPIDN DNIIAAAAAARGT	YTIPPGFNISDKNMGKEYRGQNKA INKQAYEEISKEH-----	<u>64/65</u>
BoNT/B	MPA--- FNYNDPIDNDNIIMME PPFARGT	YTIEEGFNISDKNMGKEYRGQNKA AAAAAAEEISKEHLAVYKIQMCKS VK	<u>66/67</u>
BoNT/B	MPVTINNFR----- MMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAY-----AAAAAAIQMCKSVK	<u>68/69</u>
BoNT/C1	M----- SDPVDNKNILYLDTHL NTLA	NIPKSNLNVLFMGQNLNRPALRK VNPENMLAAA--- CHKAIDGRSLYNK	<u>70/71</u>
BoNT/D	MTRPVKD--- DPVNDNDILYLRIPQN KLI	YTIRDGFNLTNKGFNIESGQNIER NPALQKL-----DLPPKVCLRLTK	<u>72/73</u>
BoNT/E	MPKINSPPNYNDPVND RTILYIKPGGCQEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLVKKAAAAACKNIVSVKGIR K	<u>74/75</u>
BoNT/E	MPKINSFNYNDPAAA ANDRTILYIKPGGCQE FY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLV---HRFCKNIVSVKGIRK	<u>76/77</u>
BoNT/E	MPKINSFNYNDPVNDR TILKIKPGGCKEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLPP-----	<u>78/79</u>
BoNT/F	MP----- NYNDPVNDTILYMQI PYEEKS	TVSEGFNIGNLAVNNRGQSIKLN KIIDSIPDKGAAAAAA--CKSVIPRK	<u>80/81</u>
BoNT/G	MPVNIPP--- DPINDDIIMMEPFND PGP	QNEGFNIASKNLKTEFNGQNKAVN KEAY-----AAAAAA	<u>82/83--</u>

Please replace paragraph [00282], beginning on page 68 with the following paragraph:

--Examples of amino acid sequence deletions include the removal of one or more contiguous or non-contiguous amino acids from the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain sequence. Some examples of amino acid sequence deletions are indicated by dashes in the sequences shown in Table 5.

Table 5

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	M----- YKDPVNGVDIAYIKIP	GFNLRNTNLAANFNGQNTTEINNMNFT	<u>84/85</u>

	NAGQM	KLKNFTGLFEFYK-----	
BoNT/A	MPFVNKQ----- VNGVDIAYIKIPNAGQ M	GFNLRNTNLAANFNGQNTTEINNMNFT KLK-----LLCVRGIITSK	<u>86/87</u>
BoNT/A	MPFVNKQFNYKDP----- -AYIKIPNAGQM	GFNLRNTNLAANFNGQNTTEINNMN---- ----GLFEFYKLLCVRGIITSK	<u>88/89</u>
BoNT/A	MPFVNKQFNYKDPVN GVDIA-----	GFNLRN----- NTEINNMNFTKLKNFTGLFEFYKLLCV RGIITSK	<u>90/91</u>
BoNT/B	MPVTINNFNYNDPIDN DNIIMME-----	YTI----- ISDKNMGKEYRGQNKAINKQAYEEISK EHLAVYKIQMCKSVK	<u>92/93</u>
BoNT/B	MPVTINNFNYND----- ---EPPFARGT	YTIEEGFNISD----- GQNKAINKQAYEEISKEHLAVYKIQM CKSVK	<u>94/95</u>
BoNT/B	MP----- NDPIDNDNIIMMEPPF ARGT	YTIEEGFNISDKNMGKEYRGQNKAINK QA-----KIQMCKSVK	<u>96/97</u>
BoNT/C1	MPI----- SDPVDNKNILYLDTHL NTLA	NIPKSNLNVLFMGQNLSRNPALRKV---- -----KFCHKAIDGRSLYNK	<u>98/99</u>
BoNT/D	MTW----- VNDNDILYLRIQNKLI	YTIRDGFNLTNKGFNISGQNIERNPA -----DLFTKVCLRLTK	<u>100/101</u>
BoNT/E	MP----- DPVNDRTILYIKPGGC QEFY	GYNINNLKVNFRGQNANLNPRIITPI---- -----RFCKNIVSVKGIRK	<u>102/103</u>
BoNT/E	MPKINSFNYN----- IKPGGCQEFY	GYNINN----- GQNANLNPRIITPITGRGLVKKIIRFCK NIVSVKGIRK	<u>104/105</u>
BoNT/E	MPKINSFNYNPVDNR TILYIK-----	GYNINNLKVNFRGQNANLNPRIITPITG RGLVKKIIR-----KGIRK	<u>106/107</u>
BoNT/F	MPVAINSFNYPVDN DDTILYMQIP-----	TVSEGFNIGNLAVNNRGQSIKLNPKIID SIPD-----KFCKSVIPRK	<u>108/109</u>
BoNT/G	M-----	QNEGFNIASKNLKTEFNGQNKAVNKE A-----RIAMCKPVMYK	<u>110--</u>

Please replace paragraph [00289], beginning on page 71 with the following paragraph:

--A chimeric botulinum toxin can be constructed such that a C-terminal portion of the light chain of one botulinum toxin serotype replaces a similar C-terminal portion within the light chain of another botulinum toxin serotype. For example, the last twenty two amino acid residues bearing the dileucine motif from the C-terminus of the light chain of BoNT/A can replace the last

twenty two amino acid residues of the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

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MPKINSFNYNDPVNDRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLKN
GDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQFH
IGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSPE
YSFRFNDNSMNEFIQDPALTMHELIHSLHGLYGAKGITT KYTITQKQNPLITNIRGTNIEEF
LTFGGTDLNIITSAQSNDIYTNNLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKDA
SGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGYN
INNLRVNFGRGQANLNPRITPITGKNFTGLFEFYKLLCVRGIITSK (SEQ
ID NO:111)--
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Please replace paragraph [00291], beginning on page 72 with the following paragraph:

--In a further example, the first thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first thirty amino acid residues of the N-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

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MPFVNKQFNYKDPVNGVDIAIYIKIPNAGQMGRYYKAFKITDRIWIIPERYTFGYKPEDFN
KSSGIFNRDVC EYDPDYLTNDKKNIFFQTLIKLFNRIKSKPLGEKLLEMIINGIPYLGDRR
VPLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFA SREGF
GGIMQMKFCPEYVSFVFNQENKGASIFNRRGYFSDPALILMHELIHVLHGLYGIKVDDL P
IVPNEKKFFMQSTDTIQAEELYTFGGQDPSIISPSTDKSIYDKVLQNFRGIVDRNLNKVLV CIS
DPNININIKNFKDKYKFVEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYF
SDSLPPVKIKNLLDNEIYTIIEGFNISDKNMGKEYRGQNKAINKQAYEEISKEHLAVYKIQM
CKSVK (SEQ ID NO:112)--
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Please replace paragraph [00293], beginning on page 72 with the following paragraph:

--Still further, the chimeric construct can have both N-terminal and the C-terminal replacements. For example, the first nine amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first nine amino acid residues of the N-terminus of the light chain of BoNT/E. Additionally, in the same construct, the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

```
MPFVNKQFNNDPVNDRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLK
NGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQF
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HIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSP
EYSFRFNDNSMNEFIQDPALTMHELHSLHGLYGAKGITTKEYTITQKQNPLITNIRGTNIEE
FLTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKD
ASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGY
NINNLKVNFRGQANLNPRIITPITGKNFTGLFEFYKLLCVRGIITSK (SEQ
ID NO:113)--

Please replace paragraph [00295], beginning on page 73 with the following paragraph:

--Similarly, the first nine amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first nine amino acid residues of the N-terminus of the light chain of BoNT/B. Additionally, in the same construct, the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPFVNKQFNYNDPIDNDNIIMMEPPFARGTGRIYKAFKITDRIWIIPERYTFGYKPEDFNK
SSGIFNRDVCEYYDPDYLNTNDKKNIFFQTLIKLFNRIKSKPLGEKLEMIINGIPYLGDRRV
PLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFAFASREGFG
GIMQMKFCPEYVSFVFNQENKGASIFNRRGYFSDPALILMHELHVLHGLYGIVKVDLPI
VPNEKKFFMQSTDITQAEELYTFGGQDPSIISPSTDKSIYDKVLQNFGRGIVDRLNKVLVCISD
PNININIKYKFKDKYKFVEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYFS
DSLPPVKIKNLLDNEIYTIIEGFGNISDKNMGKEYRGQNKAINKQKNFTGLFEFYKLLCVR
GIITSK (SEQ ID NO:114)--

Please replace paragraph [00299], beginning on page 74 with the following paragraph:

--In some embodiments, a light chain can be engineered such that one or more segments of the light chain of one or more toxin serotypes replace one or more segments of equal or unequal length within the light chain of another toxin serotype. In a non-limiting example of this kind of chimeric construct, fifty amino acid residues from the N-terminus of the light chain of BoNT/A can replace eight amino acid residues of the N-terminus of the light chain of BoNT/B, resulting in a net gain of forty-two amino acids in length in the N-terminal region of the light chain chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPFVNKQFNYKDPVNGVDIAIYKIPNAGOMQPVKAFKIHNKIWWIPERDTFYNDPIDN
DNIIMMEPPFARGTGRIYKAFKITDRIWIIPERYTFGYKPEDFNKSSGIFNRDVCEYYDPDYL
LNTNDKKNIFFQTLIKLFNRIKSKPLGEKLEMIINGIPYLGDRRVPLEEFNTNIASVTVNKLIS
NPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFAFASREGFGGIMQMKFCPEYVSFVFN

VQENKGASIFNRRGYFSDPALILMHელიHVLHGLYGIVDDLPVPNEKKFFMQSTDTIQAE
 ELYTFGGQDPSIISPSTDKSIYDKVLQNFRGIVDRNLKVLVCISDPNININIKNFKDKYKF
 VEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYFSDSLPPVKIKNLLDNEIYTI
 EEGFNISDKNMGKEYRGQNKAINQAYEEISKEHLAVYKIQMCKSVK
 (SEQ ID NO:116)

Please replace paragraph [00301] beginning on page 75 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace fifteen amino acid residues within the C-terminus of the light chain of BoNT/E, resulting in a net gain of thirty-five amino acids in the C-terminal region of the light chain chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYNPVDNRILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLKN
 GDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQFH
 IGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSPE
 YSFRFNDNSMNEFIQDPALTMHELIHSLHGLYGAKGITT KYTITQKQNPLITNIRGTNIEEF
 LTFGGTDLNIITSAQSNDIYTLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKDA
 SGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGYN
 INNLKVNFRGQANLNPRIITPGFNLRNTNLAANFNGONTEINNMNFTKLKNFTGLFEF
YKLLCVRGIITSKNIVSVKGIRK
 (SEQ ID NO:117)--

Please replace paragraph [00303] beginning on page 76 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/E, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYPFVNKQFNKYKDPVNGVDIAYIKIPNAGOMYIKPGGCQEFYKSFNIMKNI
 WIIPERNVIGTTPQDFHPPTSLKNGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGI
 LLEELSKANPYLGNDNTPDNQFHIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNI
 SLRNNYMPSNHGFGSIAIVTFSPEYSFRFNDNSMNEFIQDPALTMHELIHSLHGLYGAKGI
 TTKYTITQKQNPLITNIRGTNIEEFLTFGGTDLNIITSAQSNDIYTLLADYKKIASKLSKVQV
 SNPLLNPYKDVFEAKYGLDKDASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYI
 GQYKYFKLSNLLNDSIYNISEGFNLRNTNLAANFNGONTEINNMNFTKLKNFTGLFEFY

KLCCVRGIITSK (SEQ ID NO:118)

Please replace paragraph [00305] beginning on page 76 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/B, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVTINNFMMPFVNKQFNYKDPVNGVDIAIYIKIPNAGOMIMMEPPFARGTGRIYYKAFKI
 TDRIWIIPERYTFGYKPEDFNKSSGIFNRDVCEYYDPDYLNTNDKKNIFFQTLIKLFNRIKSK
 PLGEKLEMIINGIPYLGDRRVPLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPV
 LNETIDIGIQNHFAFREGFGGIMQMKFCPEYVSFNNVQENKGASIFNRRGYFSDPALIL
 MHELIHVLHGLYGIVDDLPVPNEKKFFMQSTDTIQAEELYTFGGQDPSIISPSTDKSIYDK
 VLQNFGRGIVDRLNKVLVCISDPNININIKNKFCDKYKFVEDSEGKYSIDVESFNKLYKSLM
 LGFTEINIAENYKIKTRASYSFSDSLPPVKIKNLLDNEIGFNLRNTNLAANFNGONTEINNM
NFTKLKNFTGLFEFYKLLCVRGIITSK (SEQ ID NO:119)--

Please replace paragraph [00307] beginning on page 77 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/F, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/F. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVAINSFNMPFVNKQFNYKDPVNGVDIAIYIKIPNAGOMLYMQIPYEEKSKKYYKAFEI
 MRNVWIIPERNITGTNPSPDFDPPASLKNSSAYYDPNYLTDAEKDRYLKTTIKLFKRINSN
 PAGKVLLQEISYAKPYLGNDHTPIDFSPVTRTTSVNIKLSNVESSMLLNLLVLGAGPDIFE
 SCCYPVRKLIDPDVVYDPSNYGFGSINIVTFSPEYETFNDISGGHNSSTESFIADPAISLAHE
 LIHALHGLYGARGVTYEETIEVKQAPLMIAEKPIRLEEFLTFGGQDLNIITSAMKEKIYNLL
 ANYEKIATRLSEVNSAPPEYDINEYKDYFQWKYGLDKNADGSYTVNENKFNEIYKKLYSF
 TESDLANKFKVKCRNTYFIKYEFLKVPNLLDDDIYGFNLRNTNLAANFNGONTEINNMN

FTKLKNFTGLFEFYKLLCVRGIITSK (SEQ ID NO:120)--

Please replace paragraph [00309] beginning on page 78 with the following paragraph:

--In some embodiments, the swapped sequences can be derived from two different serotypes, resulting in a chimera with regions from three different serotypes in all. In this example, eight amino acid residues from the N-terminus of the light chain of BoNT/B can replace five amino acid residues of the N-terminus of the light chain of BoNT/E, resulting in a net gain of three amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, 30 amino acid residues including the dileucine repeat of the C-terminus of the light chain of BoNT/A can replace ten amino acid residues within the C-terminus of the light chain of BoNT/E, resulting in a net gain of 20 amino acids in the C-terminal region of the chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYNDPVTINWFNYDRITILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHP
PTSLKNGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNT
PDNQFHIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAI
VTFSPEYSFRFNDNSMNEFIQDPALTMHELIHSLHGLYGAKGITT KYTITQKQNPLITNIRG
TNIEEFLTFFGGTDLNIITSAQSNDIYTNNLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYG
LDKDASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYN
ISEGYNINNLKVNFRGQANLNPRIITPITGRGLVKKIIRFCKNNMNF**FTKLKNFTGLFEFY**
KLLCVRGIITSK

(SEQ ID NO:121)--

Please replace paragraph [00311] beginning on page 78 with the following paragraph:

--In a non-limiting example, eight amino acid residues from the N-terminus of the light chain of BoNT/B can replace five amino acid residues of the N-terminus of the light chain of BoNT/F, resulting in a net gain of three amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, 30 amino acid residues including the dileucine repeat of the C-terminus of the light chain of BoNT/A can replace ten amino acid residues within the C-terminus of the light chain of BoNT/F, resulting in a net gain of 20 amino acids in the C-terminal region of the chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVAINSFNYNDVTINNFNYTILYMQIPYEEKSKKYYKA FEIMRNVWIIPERNTIGTNPSDF
DPPASLKNGSSAYYDPNYLT TDAEKDRYLKTTIKLFKRINSNPAGKVLLQEISYAKPYLGN
DHTPIDEFSPVTRTTSVNIKLSTNVESSMLLNLLVLGAGPDIFESCCYPVRKLIDPDVVYDPS
NYGFGSINIVTFSPEYEYTFNDISGGHNSSTESFIADPAISLAHELIHALHGLYGARGVTYEE
TIEVKQAPLMIAEKPIRLEEFLTFGGQDLNIITSAMKEKIYNNLLANYEKIATRLSEVNSAPP
EYDINEYKDYFQWKYGLDKNADGSYTVNENKFNEIYKKLYSFTESDLANKFKVKCRNTY
FIKYEFLKVPNLLDDDIYTVSEGFNIGNLAVNNRGQSIKLNPKIIDSIPDKGLVEKNNMNFT
KLKNFTGLFEFYKLLCVRGIITSKRK (SEQ ID NO:122)--